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14. ABSTRACT

The primary long-term objective of this research is to understand how chemokine signaling through MAPK influences progression of breast carcinoma cells to a hormone-independent, endocrine therapy resistant and metastatic phenotype. Our preliminary evidence demonstrates that over expression of CXCR4 in breast carcinoma cells leads to a hormone independent phenotype in vivo. It was also determined by our lab that human mesenchymal stem cells in contact with breast cancer cells (MCF7 cell line) could induce proliferation and lead to hormone independent tumors in vivo. Upon analysis of these tumors by real-time PCR, it was found that the MSC containing tumors had increased gene transcription of progesterone receptor as well as SDF-1 indicating ER crosstalk. Future studies are planned to look more closely at the mechanisms involved in this MSC-tumor cell interaction, specifically identifying a role for SDF-1. We propose SDF-1 is the primary factor involved, either being secreted by the MSCs or the MSCs are stimulating its production in the carcinoma cells themselves. Future plans involve using MSCs as source for SDF-1 to test previously outlined objectives.

15. SUBJECT TERMS
Breast cancer, chemokine, SDF-1, MSC

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Table of Contents

Page

INTRODUCTION

The development of resistance to anti-estrogens and the progression to hormone-independence are still poorly understood problems in the treatment of ER-positive breast cancers. The function of the ER-coegulated proteins and crosstalk with the ER signal pathway, growth factor mediated signaling, and other kinase networks could be responsible for this resistance. It has been shown that some chemokines lead to the initiation of migration. One such chemokine, stromal-derived growth factor 1 (SDF-1/CXCL12) along with its receptor chemokine X receptor 4 (CXCR4) expression is a critical component in the ability of cancer cells to invade and metastasize. It has been demonstrated that estrogen-estrogen receptor (ER) is able to mediate the upregulation of SDF-1 thereby establishing a link between hormone and chemokine signaling in proliferation of breast carcinoma cells. This SDF1-CXCR4 axis functions to stimulate proliferation, promote cell motility/invasion, and suppress apoptosis through activation of specific downstream signaling pathways. Our previously outlined objectives sought to test one such pathway including phosphatidylinositol 3-kinase (PI3K)/AKT and members of the mitogen-activated protein kinase (MAPK) family (Erk1, and p38) because both MAPKs and PI3K/AKT have been implicated in development of endocrine therapy resistance in breast carcinoma.

More recently, our lab became interested in the concept of human mesenchymal stem cells and their ability to contribute to the tumor microenvironment. Preliminary studies have shown that MSCs home to sites of breast cancer and integrate into the tumor stroma. We have shown that MSCs enhance primary tumor growth as well as promote hormone-independent tumor growth of the estrogen receptor positive, hormone-dependent breast carcinoma cell line MCF-7 in immunocompromised mice. This is correlated with increase expression of SDF-1, Vascular Endothelial Growth Factor (VEGF), and Progesterone Receptor (PR) in the presence of MSCS as compared to MCF-7 only tumors. Recognizing that SDF-1, VEGF, and PR are all ER mediated genes led us to further investigate the possibility of MSC crosstalk with the ER. We suggest that it is this increase in SDF-1 that acts in a paracrine fashion on the breast cancer cells through its receptor, CXCR4, leading to a shift to hormone independent growth while still remaining estrogen sensitive. The ability of CXCR4 to regulate estrogen receptor signaling and progression to hormone-independence represents an important area of research.

Task 1. Establish crosstalk between CXCR4/G-protein signaling and estrogen receptor (ER).

1.A Determine CXCR4 activation leads to increased ER-mediated gene expression.

Through ERE-luciferase (year 2) and RT-PCR (year 1) analysis we have shown that overexpression of CXCR4 leads to increased levels of ER-mediated gene expression; specifically we found increased levels of SDF-1 and, the classic ER-mediated gene, Progesterone receptor (PgR).

1.B Determine if CXCR4 activates p38.

Western blot analysis of breast carcinoma cell lines either artificially expressing CXCR4 (MCF-7-CXCR4) or those which endogenously overexpress CXCR4 (MDA-MB-361, MDA-MB-231) demonstrated higher **basal** phophorylated levels of p38 and Erk1/2 as compared to CXCR4 null cells (MCF-7). Further investigation by western blot on MCF-7-CXCR4 and MDA-MB-361 cells treated with SDF-1 revealed a time dependent activation of p38 and Erk signaling in these CXCR4 positive cell systems. These results reveal both increased **basal** activation of MAPK signaling as well as **ligand induced** activation (year 1).

Due to a lack in the availability of a p38-MAPK-luciferase (originally proposed), we used the ERE-luciferase assay in conjunction with specific chemical inhibitors to PI3K (LY294002), p38 (SB203580), and MAPK (UO126). Our results show the same increase in ERE activity of the MCF-7-CXCR4 cells over their vector counterparts. Through these experiments we also found that by blocking PI3K, p38 or MAPK there is a decrease in CXCR4s ability to activate ER transcription (year 2).

1.C Determine if p38-MAPK signaling is required for CXCR4 mediated breast cancer progression.

The originally proposed experiment to test the requirement of p38-MAPK in CXCR4 signaling was addressed in the revision of 1.B.2. Therefore, we utilized our immunocompromised animal model to test the ability of specific inhibitors of p38 (RWJ 67657) and Erk1/2 (PD184135) to inhibit the ability of CXCR4 expression to induce hormone-independent growth. These findings indicate p38 activation is required in CXCR4 mediated activation of ER and hormone independent tumor growth (year 2).

We used an additional breast carcinoma line, MDA-MB-361, which has endogenously high levels of CXCR4 to test the effect of p38 in our in vivo model system. Validating our observation with the MCF-7-CXCR4 cells, both Erk and p38 inhibition significantly reduced tumor volume in these animals, only inhibition of p38 reduced tumor volume to the level of the pure anti-estrogen ICI 182,780 (fulvestrant) (year 2).

We then looked at the SDF-1 effect on endocrine resistant tumors by injecting MCF7-CXCR4 cells into immunocompromised ovariectomized mice and treating with a single

dose of ICI (day 7 post injection). As expected ICI treatment decreased tumor volume in these animals. However, mice injected with MCF-7-CXCR4 cells mixed with Matrigel including SDF-1 (100ng) were able to overcome ICI treatment, and continues to increase in tumor volume over time. This indicates that the CXCR4/SDF-1 axis drives an endocrine resistant phenotype. In addition, inhibition of p38 in this study brings tumor volumes back down to ICI levels demonstrating its vital role in this event. Inhibition of Erk also decreased the initial ability of SDF-1 treatment to overcome the effect of ICI, but was unable to sustain this effect over time (year 2).

Take together these results demonstrate a role for SDF-1 and CXCR4 in the progression to hormone independence as well as endocrine resistance. We also clearly demonstrate here a role for p38 signaling in both hormone independence and endocrine resistance. Erk signaling was also shown to be involved in hormone independence, but not sufficient for endocrine resistance.

Task 2. CXCR4/SDF-1 axis regulates ERE-mediated gene expression through phosphorylation of the ER.

2.A Determine which transactivation domain (AF1 or AF2) CXCR4 signaling targets on ER.

As reported in year 1 annual summary, western blots were performed to determine the total phosphorylation of ERα AF1 and AF2 sites after stimulation with SDF-1 in both the MCF-7-CXCR4 and MDA-MB-361 cells. Our first blot showed that the AF1 domain was the site of phosphorylation following treatment with SDF-1. Yet, subsequent blots have not been able to reproduce these results. Therefore, no conclusion can be drawn at this time. However, a recent publication by Sauvè *et al* report SDF-1 induces phosphorylation of the AF-1 domain of ER-beta at serine 87 (Sauve et al., 2009).

2.B Determine if CXCR4 phosphorylates the ER at specific sites.

Western blots were carried out on MCF-7-CXCR4 and MDA-MB-361 cells after treatment with SDF-1(or vehicle control) using phospho-specific antibodies to the ER. We have concluded that SDF-1 treated cells induce phosphorylation at both serine 118 and serine 167 on the ER in both cell lines (year 1).

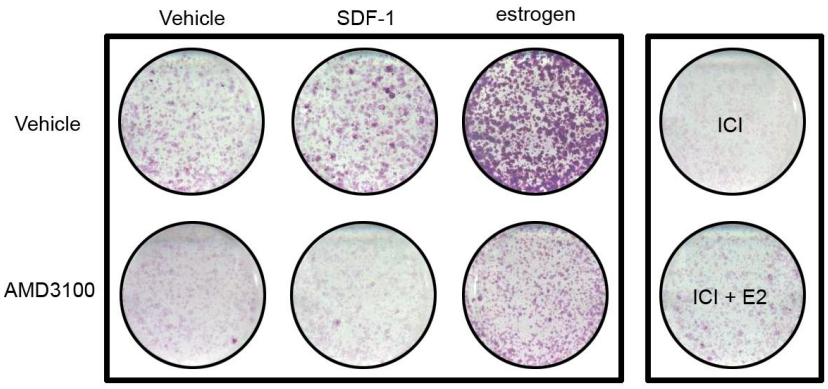
2.C Determine the requirement of ER phosphorylation by CXCR4 for mediation of gene expression.

These experiments have not yet been conducted. We plan to use phospho-mutants of the ER at sites S118 and S167 in conjunction with luciferase reporter assays to conclude if these sites are required and/or sufficient for ER activation. Mutants will be used alone and in combination. The recent report by Sauvè *et al* demonstrate the ability of phospho-mutants of ER-beta to abolish the SDF-1 induced activation of ER by similar methods (Sauve et al., 2009).

Task 3. Demonstrate CXCR4/SDF-1 axis mediated gene expression is necessary for hormone independence in breast cancer.

3.A Demonstrate that hormone independence can be disrupted by blocking the CXCR4/SDF-1 axis *in vitro*.

These studies are ongoing. Several assays have been performed using MCF-7-VEC, MCF-7-CXCR4, MDA-MD-361, and MDA-MB-231 cells. We show a stimulation of colony formation with the addition of SDF-1 even in the absence of estrogen which can be knocked down with the addition of the CXCR4 specific inhibitor, AMD3100. AMD3100 also appears to inhibit colony formation in the presence of estrogen indicating again a link between ER and CXCR4 (year 1 to present).



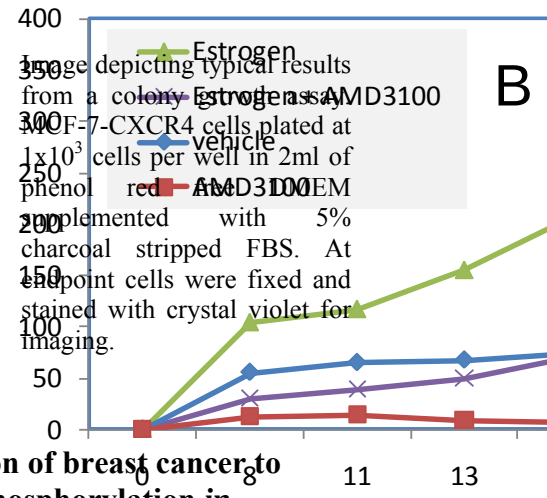
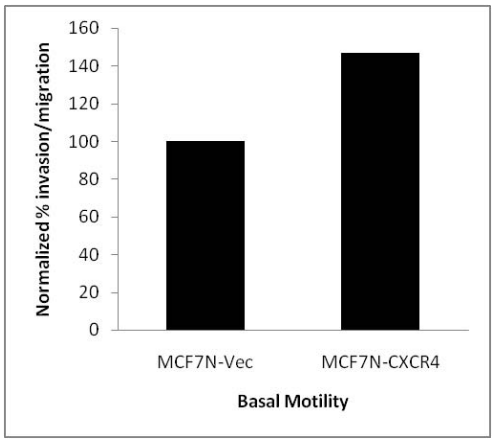
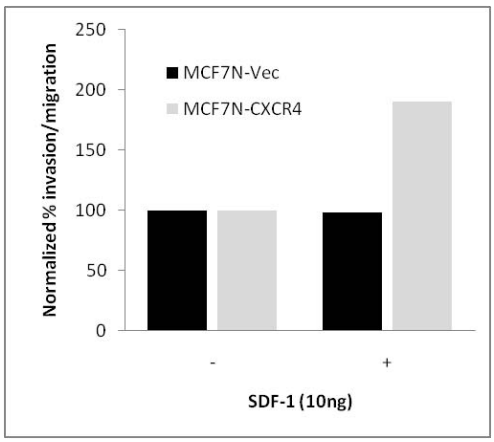


Image depicting typical results from a colony formation assay. MCF-7-CXCR4 cells plated at $1x10^3$ cells per well in 2ml of phenol red free DMEM supplemented with 5% charcoal stripped FBS. At endpoint cells were fixed and stained with crystal violet for imaging.

3.B Determine the role of CXCR4 expression on progression of breast cancer to invasive and metastatic phenotype dependent on ER phosphorylation *in vitro*.

These studies have been initiated but are not yet complete. Further studies will be carried out as outlined in previous annual summaries. Here we show representative figures from an invasion/migration assay in which we see enhanced basal motility of MCF-7-CXCR4 cells as well as movement toward the chemoattractant, in this case, the ligand for CXCR4, SDF-1.





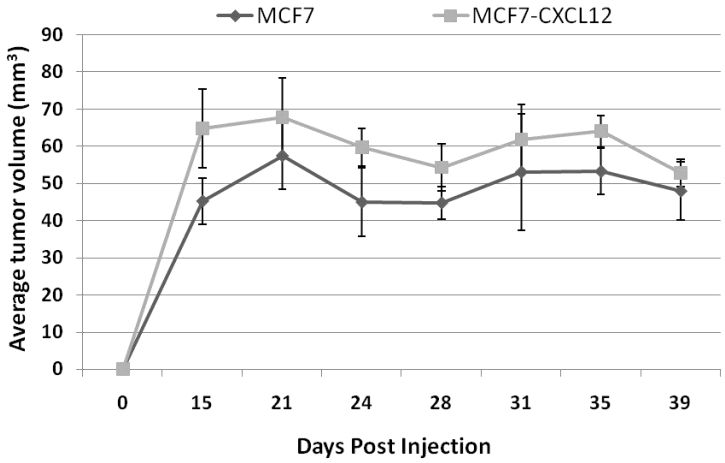
Invasion/Migration Assay. MCF-7-vector or MCF-7-CXCR4 cells were seeded in the upper chamber of a transwell insert (24 well plate format) with or without a chemoattractant in the lower wells. After 24hrs % cell invasion was calculated.

3.C Test CXCR4/SDF-1 affect on tumor formation, estrogen-independence and metastasis *in vivo*.

Primary Tumor Experiments:
Immunocompromised mouse models were utilized to evaluate tumor growth after injection of MCF-7-CXCR4 cells into the mammary fat pad of ovariectomized female mice with or without estrogen pellets. MCF-7-CXCR4 cells grew faster and larger than control tumors under both conditions. Metastases were seen in a few of the CXCR4 mice but results were not conclusive (year 1).

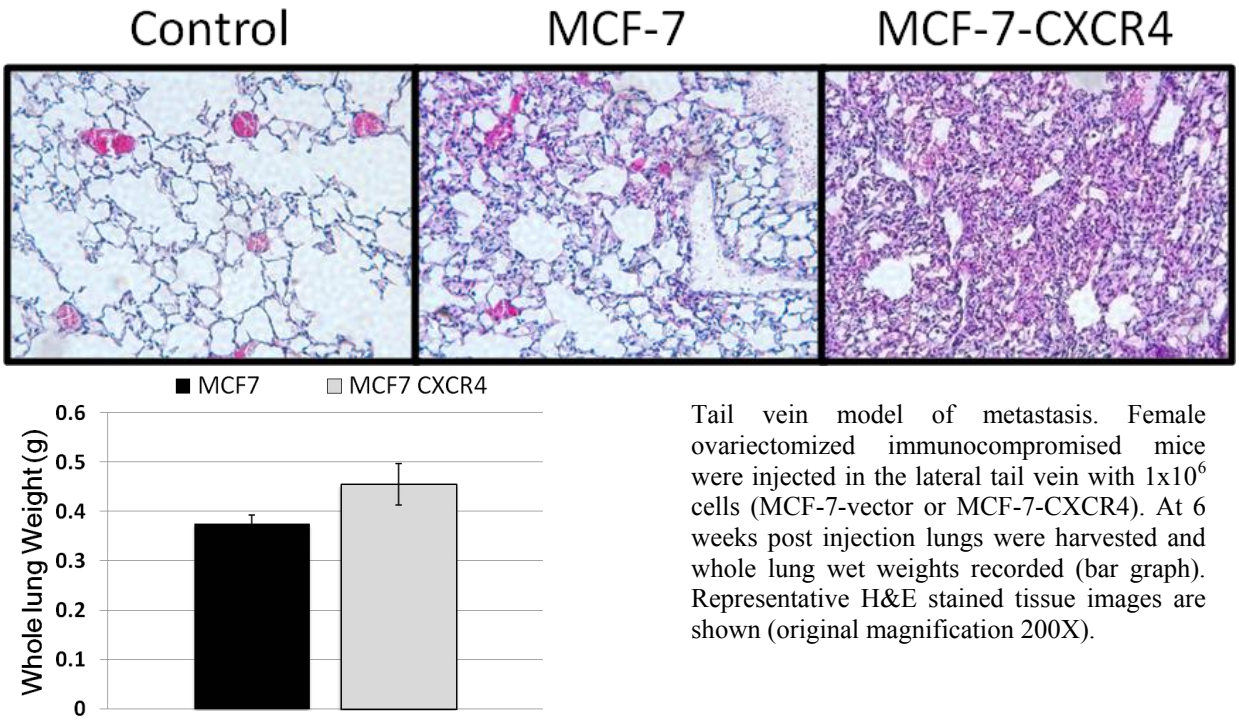
We next set out to determine if this increased tumor growth exhibited by the MCF-7-CXCR4 cells could be reversed by blocking CXCR4. Mice injected in the MFP with MCF-7-CXCR4 cells were treated with AMD3100 twice daily for 14 days after tumor formation. Treatment with the CXCR4 antagonist resulted in decreased tumor volume, effectively reversing the effects of CXCR4 overexpression in these cells. Similar results were seen with the use of a CXCR4 specific antibody. Anti-CXCR4 was able to decrease tumor volume in MCF7-CXCR4 cells (+/- estrogen) and MDA-MB-361 cells (+estrogen) (year 1).

Studies with MCF-7-SDF-1 overexpressing cell lines (see graph below) did not show a significant increase in tumor volume (year 2). We are aware that these cells have low levels of CXCR4 and that it may be because of a lack in receptor that SDF-1 overexpression was unable to exert noticeable effects. Therefore, we proposed to overexpress both SDF-1 and CXCR4 in the same cell line.



Stable cell lines expressing duel vector (vector-vector), Vector-SDF-1, vector-CXCR4, or both SDF-1 and CXCR4 (SDF-1-CXCR4) were generated (year 2). Though we have proposed to use these cell lines in our *in vivo* model, this may not be possible as preliminary *in vitro* experiments have not shown increased cell growth or survival in these cells as compared to vector controls. We believe this lack of effect is due to internalization and or down regulation of CXCR4 in the presence of abundant ligand (SDF-1). Others have shown this to be true in the case of CXCR4-SDF-1 signaling in the regulation of metastasis (Mirisola et al., 2009).

Metastasis Experiments:
Previously we had observed metastasis in a few of the mice injected with MCF7-CXCR4 cells. We have now developed a Tail Vein mouse model to specifically examine lung metastasis. $1x10^6$ cells in 50 ul PBS, either MCF7-vector or MCF7-CXCR4, were injected into the lateral tail vein of ovariectomized mice. Mice were sacrificed at 6 weeks post injection and lungs were harvested, fixed, processed and embedded in paraffin for sectioning. H&E sections revealed an increase in tumor cell number of MCF7-CXCR4 cells in the lungs compared to those of control lungs. We are in the process of quantifying these sections.



Tail vein model of metastasis. Female ovariectomized immunocompromised mice were injected in the lateral tail vein with $1x10^6$ cells (MCF-7-vector or MCF-7-CXCR4). At 6 weeks post injection lungs were harvested and whole lung wet weights recorded (bar graph). Representative H&E stained tissue images are shown (original magnification 200X).

Task 4: Determine the effects of mesenchymal stem cells on MCF-7 tumor growth *in vivo*

The overall purpose of the above aim was to better understand the role of MSCs in the breast tumor environment. MSCs are known to produce high levels of SDF-1 which we hope to then utilize these cells as a natural source of SDF-1 in our MCF-7 tumor model system in the future.

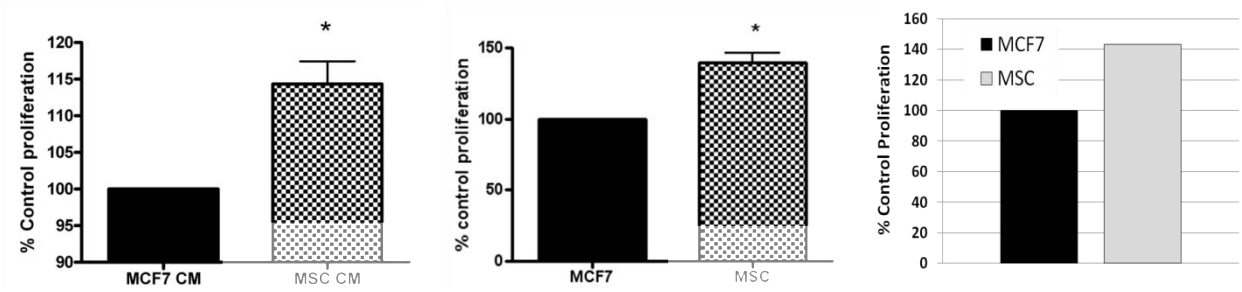
4.A Determine if Mesenchymal Stem Cells (MSC)enhance MCF-7 tumor growth in vivo.

MCF-7 cells, either alone or in combination with MSCs, were injected into immunocompromised ovariectomized female mice. Mice were also implanted with slow released estrogen pellets. Tumor volumes recorded reveals an increased growth rate of tumors derived from the mixture of MCF-7 cells with MSCs as compared to those which arose from MCF-7 cells alone. These results indicate an **increased sensitivity to estrogen** of MCF-7 cells when in the presence of MSCs (year 2).

This study was repeated but without estrogen treatment. The results were striking as MCF-7 cells formed tumors in the absence of estrogen or external factors (such as matrigel). As MCF-7 cells are hormone dependent, they will not form tumors in the absence of these factors. These results indicate an ability of MSCs to foster the promotion of **hormone independence** of MCF-7 cells *in vivo* (year 2).

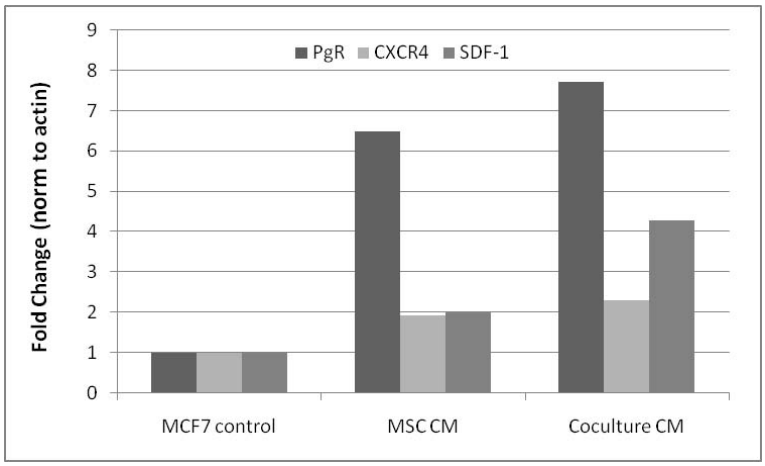
We further validated these in vivo effects through in vitro proliferation assays. MTT proliferation assays on cells treated with conditioned media from MSCs resulted in increased growth of MCF-7 cells in culture (A). MTT assays on cells grown in transwell culture (B) revealed similar results as did direct coculture assays (C) stained with ki-67. All assays show increased proliferation of MCF-7 cells grown in the presence of MSCs (year 3).

A B C



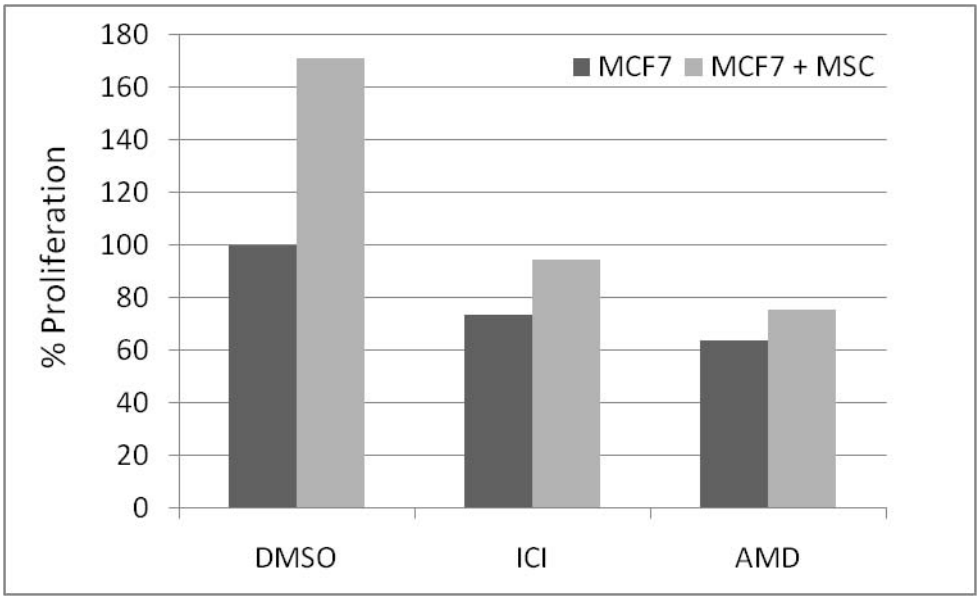
MCS induce gene expression of ER mediated genes.

MCF-7 cells were cultured in the presence of conditioned media from either MSCs grown alone, or cocultured MCF-7 and MSCs (1:1 ratio). After 24 hours, cells were harvested, RNA isolated and gene expression analyzed by real time PCR. As the graph below demonstrates, we see elevated levels for Progesterone and SDF-1, both ER regulated genes. Interestingly, we also observed increased levels of CXCR4, the receptor for SDF-1, in cells treated with either MSC or cocultured conditioned media (year 3).



Endpoint tumors from above animal studies were harvested for use in Real-time PCR analysis. As reported previously (year 2), Progesterone Receptor, SDF-1, and VEGF gene expression was upregulated in tumors containing MSCs. As these are ER mediated genes, these results indicate an ER-MSC crosstalk. Increased levels of SDF-1 led us to speculate MSC as a source of SDF-1 or stimulate an increase in SDF-1 production by the MCF-7 cells. We believe this strengthens our case for the role of SDF-1/CXCR4 in breast tumorigenesis and hormone independence.

To further examine the role of SDF-1 and CXCR4 expression in the enhancement of cell growth by MSCs, we tested the effect of inhibiting CXCR4 as well as ER. Using the transwell assay described above in conjunction with specific inhibitors to ER (ICI 182,780) and CXCR4 (AMD3100). We again see enhanced proliferation when MCF-7 cells are grown in the presence of MSCs, but this is decreased with the addition of ICI and to a greater extent AMD3100 indicating ER signaling as well as CXCR4 signaling is involved in MSC enhancement of proliferation in these cells (year 3).



KEY RESEARCH ACCOMPLISHMENTS

- Determined CXCR4 activation by SDF-1 increases ER responsive genes expression.
- Determined CXCR4 activation leads to increased levels of phosphorylated p38, both basally and ligand induced signaling.
- Determined that p38-MAPK signaling is involved in CXCR4 mediated breast cancer progression in vivo.
- Determined SDF-1 specific phosphorylation at S118 and S167on ER.
- Demonstrated SDF-1 ability to initiate increased colony formation in a hormone independent yet estrogen responsive manor.
- Demonstrated CXCR4/SDF-1 ability to enhance tumorigenesis and metastasis *in vivo*.
- Determined the ability of CXCR4/SDF1 to affect tumor formation, estrogen-independence and metastasis in vivo using a lung metastasis model.
- Generated stable cell lines overexpression SDF-1, CXCR4, or both in the MCF7 parental line.
- Discovered the ability of MSCs to increase breast cancer cell sensitivity to estrogen *in vitro* and *in vivo*.
- Determined MSCs increase breast tumor proliferation even in the absence of estrogen *in vitro* and *in vivo*.
- Discovered that MSCs promote a hormone independent phenotype in breast carcinoma *in vitro* and *in vivo*.
- Found that MSCs induce gene expression of ER mediated genes in breast tumors *in vitro* and *in vivo*.

BREAST CANCER TRAINING-RELATED OUTCOMES

2006-2007

- Successfully completed preliminary exam for the Biomedical Science Graduate Program.
- Lecturer, Endocrine Pharmacology class, Department of Pharmacology, Tulane University, New Orleans, LA
- Teaching assistant, Cellular and Molecular Biology Program, Tulane University, New Orleans, LA
- Mentorship, Shannon E. Muir, Pharmacology Masters student, Department of Pharmacology, Tulane University, New Orleans, LA

2007-2008

- Successfully completed prospectus exam for the Biomedical Science Graduate Program, Tulane University, New Orleans, LA
- Presented poster session at AACR National meeting, San Diego, CA. April 2008.
- DOD Breast Cancer Research Program Era of Hope Meeting, Baltimore, MD. June 2008, Invited Platform Session
- Attended Pathobiology workshop training on interpreting biological specimens, AACR, Snowmass, CO. July 2008.
- Mentorship, Thomas M. McCloy, Pharmacology Masters student, Department of Pharmacology, Tulane University, New Orleans, LA

2008-2009

- Attended St. Jude National Graduate Student Symposium, St. Jude Children's Hospital, Memphis, TN. April 2009.

All Years

- Weekly lab meeting/journal club, Burow Lab, Tulane University, New Orleans, LA
- Weekly attendance to Cancer Center meeting, Tulane University, New Orleans, LA
- Weekly attendance to Breast and Ovarian Group, Tulane University, New Orleans, LA

REPORTABLE OUTCOMES

Presentations:

2006-2007

"CXCR4 Drives Breast Carcinoma to Hormone-Independent and Metastatic Phenotype". Molecular and Cellular Biology Program Annual Retreat, Primate Center, Tulane University, Covington, LA. October 2006. **Lyndsay Vanhoy Rhodes**

"Chemokines in Breast Cancer". George A. Pfeiffer Science Symposium, Pfeiffer University, Misenheimer, NC. October 2006. Alumni speaker. **Lyndsay Vanhoy Rhodes**

"CXCR4 Drives Breast Carcinoma to Hormone-Independent and Metastatic Phenotype". Molecular and Cellular Biology Program Annual Research Days, Tulane University School of Medicine, New Orleans, LA. March 2007. **Lyndsay Vanhoy Rhodes**

2007-2008

"Adult human mesenchymal stem cells enhance breast cancer tumorigenesis and promote hormone independence". American Association for Cancer Research Pathobiology Workshop, Snowmass, CO. July 2008. **Lyndsay Vanhoy Rhodes**

"Adult human mesenchymal stem cells enhance breast cancer tumorigenesis and promote hormone independence". DOD Breast Cancer Research Program Era of Hope Meeting, Baltimore, MD. June 2008, Invited Platform Session. **Lyndsay Vanhoy Rhodes**

"Adult human mesenchymal stem cells enhance breast cancer tumorigenesis and promote hormone independence". American Association for Cancer Research Annual Meeting, San Diego, CA. April 2008. **Lyndsay Vanhoy Rhodes**

"Adult human mesenchymal stem cells enhance breast cancer tumorigenesis and promote hormone independence". Tulane University Health Sciences Center Research Days, Tulane University, New Orleans, LA. Mar 2008. **Lyndsay Vanhoy Rhodes**

"Human Mesenchymal Stem Cells in Breast Cancer". Center for Bioenvironmental Research joint laboratory meeting, Tulane University School of Medicine, New Orleans, LA. February 2008. **Lyndsay Vanhoy Rhodes**

2008-2009

"Adult human mesenchymal stem cells enhance breast cancer tumorigenesis and promote hormone independence". St. Jude National Graduate Student Symposium. St. Jude Children's Hospital, Memphis, TN. April 2009. **Lyndsay Vanhoy Rhodes**

Abstracts:

2006-2007

Lyndsay Vanhoy Rhodes, Alberto Salvo, Pablo Fonseca, Syreeta Tilghman, Steven Elliott, and Matthew E. Burow. "CXCR4 Drives Breast Carcinoma to Hormone-Independent and Metastatic Phenotype", Molecular and Cellular Biology Annual Research Days, Tulane University, Feb. 28 – Mar. 1, 2007, New Orleans, LA.

2007-2008

Lyndsay V. Rhodes, Shannon E. Muir, Steven Elliott, Lori M. Guillot, James W. Antoon, Patrice Penfornis, Syreeta L. Tilghman, John A. McLachlan, Brian G. Rowan, Radhika Pochampally, Matthew E. Burow. "Adult human mesenchymal stem cells enhance breast cancer tumorigenesis and promote hormone independence". AACR Annual Meeting, April, 2008.

Publications:

Rhodes, LV, Muir, SE, Elliott, S, Guillot, LM, Antoon, JW, Penfornis, P, Tilghman, SL, Salvo, VA, Fonseca, JP, Lacey, MR, McLachlan, JA, Rowan, BG, Pochampally, R, and Burow, ME. Adult human mesenchymal stem cells enhance breast carcinoma tumorigenesis and progression to hormone independence. Breast Cancer Research and Treatment. *Epub ahead of print*. (2009). DOI:10.1007/s10549-009-0458-2

CONCLUSION

The hypothesis that overexpressing CXCR4 cancer cells crosstalk with ER to upregulate their own ligand (SDF1) and form a feed-forward autocrine loop which activates CXCR4 signaling constitutively provides a novel mechanism for tumor progression and metastasis. We have shown the ability of CXCR4 signaling to increase proliferation of MCF-7 cells *in vitro* as well as *in vivo*. We have also shown the involvement of both Erk1/2 and p38 signaling in the interaction of CXCR4 and ER. Our research provides strong evidence that combining SDF1/CXCR4 blockade with current endocrine therapy strategies will be synergistically effective in treatment for endocrine resistant and metastatic breast cancer. Through our research we have also discovered that MSCs have the ability to increase proliferation and hormone independence of breast carcinoma, which we believe is achieved, at least in part, through the SDF-1/CXCR4 axis. As a novel mechanism of hormone independence, these pathways may prove to provide a unique approach to breast cancer treatment. New treatment options for patients are necessary for improved patient care.

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Honors:

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Recent Publications:

Rhodes, LV, Muir, SE, Elliott, S, Guillot, LM, Antoon, JW, Penfornis, P, Tilghman, SL, Salvo, VA, Fonseca, JP, Lacey, MR, McLachlan, JA, Rowan, BG, Pochampally, R, and Burow, ME. Adult human mesenchymal stem cells enhance breast carcinoma tumorigenesis and progression to hormone independence. Breast Cancer Research and Treatment. *Epub ahead of print*. (2009). DOI:10.1007/s10549-009-0458-2

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Recent Presentations:

"Adult human mesenchymal stem cells enhance breast cancer tumorigenesis and promote hormone independence". American Association for Cancer Research Pathobiology Workshop, Snowmass, CO. July 2008.

"Adult human mesenchymal stem cells enhance breast cancer tumorigenesis and promote hormone independence". DOD Breast Cancer Research Program Era of Hope Meeting, Baltimore, MD. June 2008, Invited Platform Session.

"Adult human mesenchymal stem cells enhance breast cancer tumorigenesis and promote hormone independence". American Association for Cancer Research Annual Meeting, San Diego, CA. April 2008.

"Adult human mesenchymal stem cells enhance breast cancer tumorigenesis and promote hormone independence". Tulane University Health Sciences Center Research Days, Tulane University, New Orleans, LA. Mar 2008.

"Human Mesenchymal Stem Cells in Breast Cancer". Center for Bioenvironmental Research joint laboratory meeting, Tulane University School of Medicine, New Orleans, LA. February 2008.

"CXCR4 Drives Breast Carcinoma to Hormone-Independent and Metastatic Phenotype". Molecular and Cellular Biology Program Annual Research Days, Tulane University School of Medicine, New Orleans, LA. March 2007.

"CXCR4 Drives Breast Carcinoma to Hormone-Independent and Metastatic Phenotype". Molecular and Cellular Biology Program Annual Retreat, Primate Center, Tulane University, Covington, LA. October 2006.

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Abstracts:

Lyndsay V. Rhodes, Syreeta L. Tilghman, Stephen M. Boue, Ashley M. Nitschke, Shuchun Wang, James W. Antoon, Jennifer Driver, Hafez Khalili, Shannon E. Muir, Steven Elliott,

Melyssa R. Bratton, Maria C. Zimmerman, Michelle R. Lacey, Charles E. Wood, Barbara S. Beckman, John A. McLachlan, Bin Shan, Guangdi Wang, Matthew E. Burow, Bridgette M. Collins-Burow. "Glyceollin as novel targeted therapeutic for the treatment of metastatic triple negative breast cancer". Tulane University Health Sciences Center Research Days, Tulane University, New Orleans, LA. January 2009.

James W. Antoon, Martin D. White, Evelyn M. Slaughter, William D. Meacham, Steven Elliott, Lyndsay V. Rhodes, Shannon E. Muir, Tom E. Wiese, Matthew E. Burow, Barbara S. Beckman. "Sphingosine Kinase Inhibitors Block Estrogen Receptor Signaling and Breast Cancer Tumorigenesis". Tulane University Health Sciences Center Research Days, Tulane University, New Orleans, LA. January 2009.

Lyndsay V. Rhodes, Shannon E. Muir, Steven Elliott, Lori M. Guillot, James W. Antoon, Patrice Penfornis, Syreeta L. Tilghman, John A. McLachlan, Brian G. Rowan, Radhika Pochampally, Matthew E. Burow. "Adult human mesenchymal stem cells enhance breast cancer tumorigenesis and promote hormone independence". 5th Annual Women's Health Research Day, Tulane University, New Orleans, LA, December 2008.

James W. Antoon, Matthew E. Burow, C.D. Smith, Steven Elliott, Lyndsay V. Rhodes, Martin D. White, Micheal Bloch, William D. Meacham, Evelyn M. Slaughter, Barbara S. Beckman. "Sphingosine Kinase inhibitors block NF-κB signaling in chemoresistant breast cancer cells". 5th Annual Women's Health Research Day, Tulane University, New Orleans, LA, December 2008.

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Lyndsay V. Rhodes, Shannon E. Muir, Steven Elliott, Lori M. Guillot, James W. Antoon, Patrice Penfornis, Syreeta L. Tilghman, John A. McLachlan, Brian G. Rowan, Radhika Pochampally, Matthew E. Burow. "Adult human mesenchymal stem cells enhance breast cancer tumorigenesis and promote hormone independence". Tulane University Health Sciences Center Research Days, Tulane University, New Orleans, LA. March 2008.

Shannon Muir, Lyndsay Vanhoy-Rhodes, Yun Zhu, Virgilio A. Salvo, Steven Elliott, Lori Guillot, Juan P. Fonseca, John A. McLachlan, Brian Barnett, Barbara S. Beckman, Tyler J. Curiel, Matthew E. Burow. "The chemokine receptor CXCR7 mediates estrogen-stimulated breast cancer tumorigenesis". AACR Annual Meeting, April, 2008.

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breast cancer tumorigenesis". Tulane University Health Sciences Center Research Days, Tulane University, New Orleans, LA. March 2008.

Meacham WD, Antoon JW, Burow ME, Smith CD, Slaughter EM, Rhodes LV, Muir SE, Guillot LM, Bratton MR, Beckman BS. "Effect of Novel Sphingosine Kinase Inhibitors on Estrogen Receptor in Endocrine Sensitive and Endocrine Resistant Breast Cancer". Tulane University Health Sciences Center Research Days, Tulane University, New Orleans, LA. March 2008.

Antoon JW, Meacham WD , Burow ME, Smith CD, Slaughter EM, Rhodes LV, Muir SE, Guillot LM, Bratton MR, Beckman BS. "Effect of Novel Sphingosine Kinase Inhibitors on Estrogen Receptor in Endocrine Sensitive and Endocrine Resistant Breast Cancer". Louisiana Cancer Research Consortium, New Orleans, LA. August 2008.

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